

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
23 June 2005 (23.06.2005)

PCT

(10) International Publication Number
WO 2005/056596 A1

(51) International Patent Classification⁷: **C07K 14/705, G06F 19/00**

(21) International Application Number:
PCT/IB2004/004335

(22) International Filing Date: 6 December 2004 (06.12.2004)

(25) Filing Language: **English**

(26) Publication Language: **English**

(30) Priority Data:
0328261.3 5 December 2003 (05.12.2003) GB

(71) Applicants (*for all designated States except US*): **UNIVERSITY OF GRONINGEN [NL/NL]**; Antonius Deusinglaan 1, NL-9713 AV Groningen (NL). **EUROPEAN MOLECULAR BIOLOGY LABORATORY [DE/DE]**; Meyerhofstrasse 1, 69117 Heidelberg (DE). **NATIONAL UNIVERSITY OF IRELAND [IE/IE]**; Galway, University Road, Galway City (IE).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **TUR, Vicente, R.** [ES/DE]; Structural Biology and Biocomputing Program, EMBL, Meyerhofstrasse 1, 69117 Heidelberg (DE). **VAN DER SLOOT, Albert, Martinus** [NL/NL]; Department of Pharmaceutical Biology, University of Groningen,

Antonius Deusinglaan 1, NL-9713 AV Groningen (NL). **MULLALLY, Margaret, M.** [IE/NL]; Department of Pharmaceutical Biology, University of Groningen, Antonius Deusinglaan 1, NL-9713 AV Groningen (NL). **COOL, Robert, H.** [NL/NL]; Department of Pharmaceutical Biology, University of Groningen, Antonius Deusinglaan 1, NL-9713 AV Groningen (NL). **SZEGEZDI, Eva, E.** [HU/IE]; Cell Stress & Apoptosis Research Group, Department of Biochemistry, National University of Ireland, Galway (IE). **SAMALI, Afshin** [IE/IE]; Cell Stress & Apoptosis Research Group, Department of Biochemistry, National University of Ireland, Galway (IE). **FERNANDEZ-BALLESTER, Gregorio** [ES/DE]; Structural Biology and Biocomputing Program, EMBL, Meyerhofstrasse 1, 69117 Heidelberg (DE). **SERRANO, Luis** [ES/DE]; Structural Biology and Biocomputing Program, EMBL, Meyerhofstrasse 1, 69117 Heidelberg (DE). **QUAX, Wilhelmus, J.** [NL/NL]; Department of Pharmaceutical Biology, University of Groningen, Antonius Deusinglaan 1, NL-9713 AV Groningen (NL).

(74) Agents: **GOODFELLOW, Hugh, R.** et al.; Carpmaels & Ransford, 43-45 Bloomsbury Square, London WC1A 2RA (GB).

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM,

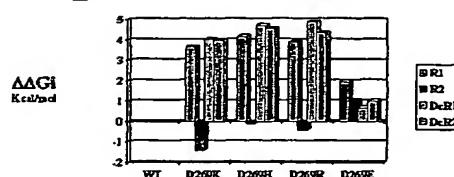
[Continued on next page]

(54) Title: IMPROVED CYTOKINE DESIGN

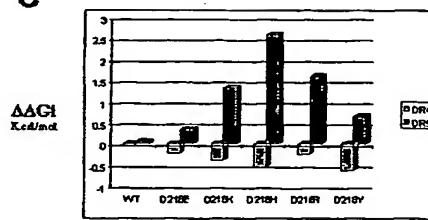
A



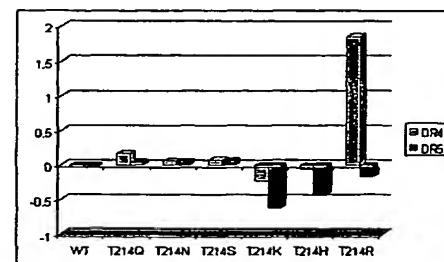
B



C



D



WO 2005/056596 A1

(57) Abstract: The present invention relates to novel methods for the design of proteins, in particular, cytokines. These methods allow the stabilisation of such cytokines, as well as modification of their selectivity/specificity for their cognate receptors. The invention also relates to various modified proteins that have been designed by the methods of the invention.



AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,

FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.